hereditary hyperekplexia

Hereditary hyperekplexia is a condition in which affected infants have increased muscle tone (hypertonia) and an exaggerated startle reaction to unexpected stimuli, especially loud noises. Following the startle reaction, infants experience a brief period in which they are very rigid and unable to move. During these rigid periods, some infants stop breathing, which, if prolonged, can be fatal. This condition may explain some cases of sudden infant death syndrome (SIDS), which is a major cause of unexplained death in babies younger than 1 year. Infants with hereditary hyperekplexia have hypertonia at all times, except when they are sleeping.

Other signs and symptoms of hereditary hyperekplexia can include muscle twitches when falling asleep (hypnagogic myoclonus) and movements of the arms or legs while asleep. Some infants, when tapped on the nose, extend their head forward and have spasms of the limb and neck muscles. Rarely, infants with hereditary hyperekplexia experience recurrent seizures (epilepsy).

The signs and symptoms of hereditary hyperekplexia typically fade by age 1. However, older individuals with hereditary hyperekplexia may still startle easily and have periods of rigidity, which can cause them to fall down. Some individuals with this condition have a low tolerance for crowded places and loud noises. Some affected people have persistent limb movements during sleep. Affected individuals who have epilepsy have the disorder throughout their lives.

Frequency

The exact prevalence of hereditary hyperekplexia is unknown. This condition has been identified in more than 70 families worldwide.

Genetic Changes

At least five genes are associated with hereditary hyperekplexia. Most of these genes provide instructions for producing proteins that are found in nerve cells (neurons). They play a role in how neurons respond to a molecule called glycine. This molecule acts as a neurotransmitter, which is a chemical messenger that transmits signals in the nervous system. Gene mutations that cause hereditary hyperekplexia disrupt normal cell signaling in the spinal cord and the part of the brain that is connected to the spinal cord (the brainstem).

Approximately 80 percent of cases of hereditary hyperekplexia are caused by mutations in the *GLRA1* gene. The *GLRA1* gene provides instructions for making one part, the alpha (α)1 subunit, of the glycine receptor protein. *GLRA1* gene mutations lead to the

production of a receptor that cannot properly respond to glycine. As a result, glycine is less able to transmit signals in the spinal cord and brainstem. Mutations in the other four genes account for a small percentage of all cases of hereditary hyperekplexia.

A disruption in cell signaling caused by mutations in the five genes associated with hereditary hyperekplexia is thought to cause the abnormal muscle movements, exaggerated startle reaction, and other symptoms characteristic of this disorder.

Inheritance Pattern

Hereditary hyperekplexia has different inheritance patterns.

This condition can be inherited in an autosomal dominant pattern, which means one copy of the altered gene in each cell is sufficient to cause the disorder. In some cases, an affected person inherits the mutation from one affected parent. Other cases may result from new mutations in the gene. These cases occur in people with no history of the disorder in their family.

Hereditary hyperekplexia can also be inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive disorder typically each carry one copy of the altered gene, but do not show signs and symptoms of the disorder.

Rarely, hereditary hyperekplexia is inherited in an X-linked pattern. In these cases, the gene associated with this condition is located on the X chromosome, which is one of the two sex chromosomes. In females (who have two X chromosomes), a mutation in one of the two copies of the gene in each cell is sufficient to cause the disorder. In males (who have only one X chromosome), a mutation in the only copy of the gene in each cell causes the disorder. A characteristic of X-linked inheritance is that fathers cannot pass X-linked traits to their sons.

Other Names for This Condition

- congenital stiff-man syndrome
- congenital stiff-person syndrome
- familial hyperekplexia
- hyperekplexia
- startle syndrome
- STHE
- stiff-baby syndrome

Diagnosis & Management

Genetic Testing

- Genetic Testing Registry: Early infantile epileptic encephalopathy 8
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C1845102/
- Genetic Testing Registry: Hyperekplexia hereditary
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C1835614/

Other Diagnosis and Management Resources

- GeneReview: Hyperekplexia
  https://www.ncbi.nlm.nih.gov/books/NBK1260

General Information from MedlinePlus

- Diagnostic Tests
  https://medlineplus.gov/diagnostictests.html
- Drug Therapy
  https://medlineplus.gov/drugtherapy.html
- Genetic Counseling
  https://medlineplus.gov/geneticcounseling.html
- Palliative Care
  https://medlineplus.gov/palliativecare.html
- Surgery and Rehabilitation
  https://medlineplus.gov/surgeryandrehabilitation.html

Additional Information & Resources

MedlinePlus

- Health Topic: Epilepsy
  https://medlineplus.gov/epilepsy.html
- Health Topic: Neuromuscular Disorders
  https://medlineplus.gov/neuromusculardisorders.html
- Health Topic: Sudden Infant Death Syndrome
  https://medlineplus.gov/suddeninfantdeathsyndrome.html

Genetic and Rare Diseases Information Center

- Hereditary hyperekplexia
  https://rarediseases.info.nih.gov/diseases/3129/hereditary-hyperekplexia

Additional NIH Resources

- National Institute of Neurological Disorders and Stroke: Hypertonia Information Page
  https://www.ninds.nih.gov/Disorders/All-Disorders/Hypertonia-Information-Page

Educational Resources

- Disease InfoSearch: Hyperekplexia hereditary
  http://www.diseaseinfosearch.org/Hyperekplexia+hereditary/3551
- MalaCards: hyperekplexia
  http://www.malacards.org/card/hyperekplexia
- Washington University, St. Louis: Neuromuscular Disease Center
  http://neuromuscular.wustl.edu/mother/activity.html#hyperekplexia

Patient Support and Advocacy Resources

- National Organization for Rare Disorders (NORD)
  https://rarediseases.org/rare-diseases/hyperekplexia/

GeneReviews

- Hyperekplexia
  https://www.ncbi.nlm.nih.gov/books/NBK1260

ClinicalTrials.gov

- ClinicalTrials.gov
  https://clinicaltrials.gov/ct2/results?cond=%22hyperekplexia%22

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28hyperekplexia%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D

OMIM

- EPILEPTIC ENCEPHALOPATHY, EARLY INFANTILE, 8
  http://omim.org/entry/300607
- HYPEREKPLEXIA, HEREDITARY 1
  http://omim.org/entry/149400

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